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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,752	LOHNING, CORINNA	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2007 and 08 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,21,22 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18, 21-22, and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/809,517.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-31 were originally filed on September 10, 2003.

The claim amendment received on December 10, 2003 canceled claims 1-16 and 24-31 and amended claims 18-19 and 22-23.

The claim amendment received on November 28, 2005 amended claim 18.

The claim amendment received on July 25, 2006 canceled claims 17-23 and added new claims 32-67. However, the claim amendment was not entered (see the Notice of Non-Compliant Amendment mailed August 1, 2006).

The claim amendment received on September 1, 2006 canceled claims 17-23 and added new claims 32-67. However, the claim amendment was not entered (see the Notice of Non-Compliant Amendment mailed on February 1, 2007).

The claim amendment received on March 1, 2007 amended claims 18 and 21-22, canceled claims 17, 19-20, and 23, and added new claims 32-34.

Claims 18, 21-22, and 32-34 are currently pending and under consideration.

Election/Restrictions

2. Applicant elected Group I (claims 17, 19, and 22) with traverse in the reply filed on November 28, 2005. The traversal was found persuasive and Groups II (claim 18) and III (claims 20-21) were rejoined. Group IV (previous claim 23) is restricted from new Group I (i.e. previous claims 17-22).

3. The species requirement is withdrawn upon further consideration.

Priority

4. The present application claims status as a DIV of 09/809,517 filed March 15, 2001 (now U.S. Patent 6,753,136) which is a CON of PCT/EP00/06968 filed July 20, 2000. The present application claims foreign priority to EP 99 11 4072.4 filed July 20, 1999 and EP 00 10 3551.8 filed February 18, 2000.

5. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies have been filed in parent Application No. 09/809,517, filed on March 22, 2004.

6. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. EP 99 11 4072.4 (foreign priority), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. EP99114072.4 does not teach the two-vector system as presently claimed. Thus the priority date for the present application is February 18, 2000.

Information Disclosure Statement

7. The information disclosure statement filed August 2, 2006 is being considered by the examiner.

Sequence Compliance

8. The present application is complaint with the sequence rules (see the response received on November 8, 2007).

Invention as Claimed

9. A host cell comprising a first vector comprising a first nucleic acid sequence encoding a modified variant of a wild type coat protein of a bacteriophage wherein said modified variant consists of (a) one or more parts of said wild type coat protein of a bateriophage wherein one of said parts comprises at least that part which causes or allows the incorporation of said coat protein into the phage coat, (b) between one and six additional amino acid residues not present at the corresponding amino acid positions in a wild type coat protein of a bacteriophage wherein one of said additional amino acid residues is a cysteine residue, and (c) a second vector comprising a second nucleic acid sequence encoding a (poly)peptide/protein comprising a cysteine residue and variations thereof.

10. Please note: the presently claimed invention has "consisting of" language which is typically interpreted as closed. However, the modified variant as claimed "consists of" (a) one or more parts of a wild type coat protein, (b) between one and six additional amino acids, and (c) a second vector (please see the claim objection below regarding (c)). Therefore, the structure of the modified variant is considered open or partially open because the variant may have one part of a

WT coat protein, more than one part of a WT coat protein, one additional amino acid, two additional amino acids, etc.

New Objection

Claim Objections

11. Claim 22 is objected to because of the following informalities: claim 22, lines 3-13 reads "[a] host cell comprising a first vector comprising a first nucleic acid sequence encoding a modified variant of a wild type coat protein of a bacteriophage, wherein said modified variant consists of: (a) one or more parts of said wild type coat protein…, (b) between one and six additional amino acid residues…, and (c) a second vector" which is considered a grammatical error. "A host cell comprising a first vector comprising a first nucleic acid sequence encoding a modified variant of a wild type coat protein of a bacteriophage, wherein said modified variant consists of: (a) one or more parts of said wild type coat protein and (b) between one and six additional amino acid residue and a second vector". Thus indicating that the modified variant consists of (a) and (b) while the second vector is within the host cell and not part of the modified variant. Appropriate correction is required.

Withdrawn Objections

12. The objection to the drawings regarding the lack of description for Figures 8A, 8B, 9A, and 9B is withdrawn in view of the amendment to the specification received on March 1, 2007.

13. The objection to the disclosure regarding the first line of the specification is withdrawn in view of the claim amendments received on March 1, 2007.

Maintained Objection

Drawings

14. The drawings/figures are objected to because tables and sequence listings included in the specification must not be duplicated in the drawings. See 37 CFR §1.58(a) and §1.83(a). Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 CFR §§1.821-1.825 will be published as part of the patent. Applicants should amend the specification to delete any figures/drawings which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format and should further amend the specification accordingly to reflect the replacement of the drawing/figure by the appropriate SEQ ID NO:.

Appropriate correction is required.

Arguments and Response

15. Applicants' arguments directed to the objection to the drawings regarding the duplication of sequences in the drawings were considered but are not persuasive for the following reasons.

Applicants contend that 37 CFR § 1.58(a) and § 1.83(a) were amended in 2004 long after the instant application was filed therefore the instant application was fully in compliance with the requirements in force at the time of filing of the instant application.

Applicants' arguments are not convincing since the drawings duplicate sequences in the sequence listing without providing additional information. While both 37 CFR § 1.58 and § 1.83 (a) were amended on September 21, 2004, the rules presently apply to the pending application. If applicant is aware that the rules are not retroactive, the applicant is requested to provide evidence to the examiner of record. Applicant may either delete the sequences or amend the sequences to

provide additional information not found in the sequence listing (i.e. alignments, indicating individual features of the sequences, etc.).

Withdrawn Rejections

16. The rejection of claims 17-22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn upon further consideration.

17. The rejection of claims 17-20 and 22 under 35 U.S.C. 102(b) as being anticipated by Kay et al. U.S. Patent 5,747,334 issued May 5, 1998 is withdrawn in view of the claim amendments received on March 1, 2007 (i.e. two-vector system).

18. The rejection of claims 17-22 under 35 U.S.C. 102(e) as being anticipated by Deem et al. U.S. Patent 6,341,256 B1 filed March 31, 1995 is withdrawn in view of the claim amendments received on March 1, 2007 (i.e. two-vector system).

19. The rejection of claims 17-19 and 22 under 35 U.S.C. 102(e) as being anticipated by Cutler et al. U.S. Patent 6,309,642 B1 filed May 13, 1998 is withdrawn in view of the claim amendments received on March 1, 2007 (i.e. two-vector system).

20. The rejection of claims 17-22 under 35 U.S.C. 103(a) as being unpatentable over Kay et al. U.S. Patent 5,747,334 issued May 5, 1998 and Kipriyanov et al. 1994 Molecular Immunology Volume 31 Number 4 pages 1047-1058 "Recombinant single-chain Fv fragments carrying C-terminal cysteine residues: production of bivalent and biotinylated miniantibodies" is withdrawn in view of the claim amendments received on March 1, 2007 (i.e. two-vector system).

21. The rejection of claims 17-22 under 35 U.S.C. 103(a) as being unpatentable over Cutler et al. U.S. Patent 6,309,642 B1 filed May 13, 1998 and Jespers et al. U.S. Patent 6,017,732 filed September 4, 1997 is withdrawn in view of the claim amendments received on March 1, 2007 (i.e. two-vector system).

New Rejections necessitated by Amendment

Claim Rejections – 35 USC § 112

22. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection. New claim 33 (claim amendment received on March 1, 2007) reads "wherein said host cell is a bacterial, fungal, plant, insect, or mammalian host cell". While applicant has support for the various host cells (see page 12, third paragraph of the originally filed specification), applicant does not have support for utilizing fungal, plant, insect, or mammalian host cells with vectors comprising bacteriophage coat proteins for phage display.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. Claims 18, 21-22, and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al. U.S. Patent 5,427,908 issued June 27, 1995 and and Kipriyanov et al. 1994 Molecular Immunology Volume 31 Number 4 pages 1047-1058 "Recombinant single-chain Fv fragments carrying C-terminal cysteine residues: production of bivalent and biotinylated miniantibodies".

For present claim 22 (independent claim), Dower et al. teach host cells comprising two vectors wherein one vector comprises nucleic acid encoding a bacteriophage coat protein which has been fused to additional amino acids (i.e. modified variant of a wild type coat protein) and another vector comprising a nucleic acid sequence encoding a polypeptide comprising a cysteine residue (i.e. VL or VH; please refer to the entire specification particularly the abstract; column 2, lines 44-61; column 4, lines 65-67; column 5, lines 1-13; column 6, lines 1-14; columns 7-9 and 14-15). In addition, Dower et al. teach fusion of tag proteins which are about 3 to about 100 amino acids in length at the C-terminus of the VH or VL and fusion of the tag and/or VH or VL at the N-terminus of the coat protein (i.e. pIII; forms VH-tag-pIII construct; please refer to column 2, lines 14-43 and column 6, lines 1-14; column 7, lines 19-65; column 9).

For present claim 18, Dower et al. teach one vector with a fusion coat protein wherein the nucleic acid also encodes one or more peptide sequences for purification (i.e. VH or VL, tag proteins; please refer to the entire specification particularly the abstract; column 1, lines 60-67; column 2, lines 1-13; column 5, lines 38-67; column 6, lines 1-14; column 7, lines 19-65).

For present claim 21, Dower et al. teach antibodies, Fab, Fv, VH, and VL (i.e. Ig and Ig fragments; please refer to the entire specification particularly column 3, lines 18-42; column 4, lines 65-67; column 5, lines 1-13).

For present claim 32, Dower et al. teach filamentous bacteriophage coat proteins including pIII (please refer to the entire specification particularly column 2, lines 14-61; column 7, lines 54-65; column 8, lines 31-57; columns 9-10).

For present claim 33, Dower et al. teach bacterial host cells (please refer to the entire specification particularly column 1, lines 60-67).

For present claim 34, Dower et al. teach *E. coli* (please refer to the entire specification particularly column 6, lines 21-27; columns 9-10).

However, Dower et al. does not specifically teach the location of the cysteine residue (i.e. between one and six amino acids from the coat protein as presently claimed) or cysteine residues within the tag.

For present claim 22, Kipriyanov et al. teach adding a C-terminal "tag" comprising five histidines and one cysteine residue to scFv in order to chemically couple various reagents to the C-terminus of the scFv and to purify proteins via IMAC (i.e. immobilized metal affinity chromatography via polyHis; please refer to the entire reference particularly the abstract; page 1047, right column; page 1048, purification sections). In addition, Kipriyanov et al. teach that Fab have free C-terminal cysteines (i.e. VH or VL comprises cysteines; art recognized structure of VH and VL requires cysteines for disulfide bond formation; please refer to page 1047, right column; page 1056).

The claim would have been obvious because the substitution of one known element (i.e. tag with undefined sequence taught by Dower et al. utilized for purification) for another (i.e. CysHisHisHisHisHis tag taught by Kipriyanov et al. utilized for purification) would have yielded predictable results to one of ordinary skill in the art at the time of the invention. More specifically, polyHis tags were well-known in the field of protein purification at the time of filing the present invention. In addition, the ability of cysteine residues to form disulfide bonds within antibody chains and between antibody chains was also well-known at the time of filing. See KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007).

Double Patenting

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 18, 21-22, and 32-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32-41 of copending Application No. 11/680,259. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 11/680,259 are drawn to host cells comprising two vectors for phage display.

For present claim 22 (independent claim), U.S. application 11/680,259 claims an isolated host cell comprising: (a) a first vector comprising a nucleic acid sequence encoding a variant of a wild type coat protein of a bacteriophage, wherein said variant comprises: (aa) one or more parts of said wild type coat protein of a bacteriophage, wherein one of said parts comprises at least that

part which causes or allows the incorporation of said coat protein into the phage coat; and, (ab) between one and six additional amino acid residues not present at the corresponding amino acid positions in a wild type coat protein of a bacteriophage, wherein one of said additional amino acid residues is a cysteine residue, and (b) a second vector comprising one or more nucleic acid sequences encoding a (poly)peptide/protein comprising a cysteine residue (see claims 32 and 34).

For present claim 18, U.S. application 11/680,259 claims wherein said nucleic acid sequence encoding said variant of said wild type coat protein further encodes: (c) one or more peptide sequences for purification and/or detection purposes, wherein said one or more peptide sequences are fused to said variant of said wild type coat protein (see claims 36-37).

For present claim 21, U.S. application 11/680,259 claims wherein said (poly)peptide/protein comprises an immunoglobulin or a functional fragment thereof (see claims 40-41).

For present claim 32, U.S. application 11/680,259 claims wherein said bacteriophage is a filamentous bacteriophage (see claims 33 and 35).

For present claim 33, U.S. application 11/680,259 claims wherein said host cell is a bacterial, fungal, plant, insect, or mammalian host cell (see claims 38-39).

For present claim 34, U.S. application 11/680,259 claims wherein said host cell is a bacterial host cell (see claims 38-39) and the specification defines a bacterial host cell as *E. coli* (see page 12, third paragraph).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. U.S. Patent 7,049,135 and U.S. Patent 5,514,548 (both Morphosys assignee).

Future Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADS
February 20, 2008

/Jon D. Epperson/
Primary Examiner, AU 1639